tumor cell proliferation; and, drug resistance of tumor cells.

Dated: April 17, 2000.

Jack Spiegel,

Director, Division of Technology Development and Transfer, Office of Technology Transfer, National Institutes of Health.

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BILLING CODE 4140–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Government-Owned Inventions; Availability for Licensing

AGENCY: National Institutes of Health, Public Health Service, DHHS.

ACTION: Notice.

SUMMARY: The inventions listed below are owned by agencies of the U.S. Government and are available for licensing in the U.S. in accordance with 35 U.S.C. 207 to achieve expeditious commercialization of results of federally-funded research and development. Foreign patent applications are filed on selected inventions to extend market coverage for companies and may also be available for licensing.

ADDRESSES: Licensing information and copies of the U.S. patent applications listed below may be obtained by contacting Carol A. Salata, Ph.D., at the Office of Technology Transfer, National Institutes of Health, 6011 Executive Boulevard, Suite 325, Rockville, Maryland 20852–3804; telephone: 301/496–7735 ext. 232; fax: 301/402–0220; e-mail: cs253n@nih.gov. A signed Confidential Disclosure Agreement will be required to receive copies of the patent applications.

Molecular Clones With Mutated HIV GAG/POL and SIV Genes

George N Pavlakis (NCI)
Serial No. 60/173,036 filed 23 Dec 1999

The invention is a DNA construct which can be used as part of an HIV DNA vaccine or as a lentiviral vector to deliver heterologous DNA to cells. The advantage of lentiviral vectors, over retroviral vectors, is that they can transduce quiescent cells, such as terminally differentiated neurons. The advantage of the lentiviral vectors of the invention over the lentiviral vectors of the prior art are that they can be highly expressed in human or mammalian cells in the absence of any other regulatory or structural protein of HIV, including REV. The advantage of vectors based on SIV is that they are divergent from HIV–1.

The construct encodes the gag/pol region of the HIV–1 genome in which the instability regions (INS) have been removed by multiple point mutations, without changing the protein sequence. The INS are regions in the unspliced RNA which decrease the amount of expression from the RNA, a decrease which is overcome by the interaction of the HIV protein REV with the RRE (Rev Response Element) found on the RNA constructs encoding gag, pol and env of HIV–1. Under certain situations the construct can result in the formation of infectious viral particles which contain only gag and pol from HIV. These viral particles can be used as vaccines or for gene therapy.

Time-Gated Imaging With a Split-Beam Source

Ronald W. Waynant (FDA)
Serial No. 60/153,100 filed 09 Sep 1999

The present invention provides a new apparatus and methods for generating a split-beam electromagnetic source for imaging devices and methodologies. With this invention, one part of a split beam is used for generating an image of an object and another part of the split beam is used for timely capturing the generated image. The present invention offers many advantages over earlier technologies. For example: (1) switching with a short duration pulse allows for a fast time gate; (2) utilization of an electromagnetic pulse source to both image and time gate allows for easier and more precise synchronization of the time gate with the imaging source; and (3) optically switching the time gate solves the problem of jitter and inhomogeneous gating.

Identification of the Domain of Plasmodium falciparum Erythrocyte Membrane Protein (PfEMP1) that Mediates Adhesion to Chondroitin Sulfate A

Arthur Scherf *et al.* (NIAID)
Serial No. 60/152,023 filed 01 Sep 1999

Plasmodium falciparum malaria is more severe in pregnant women and causes disease in the mother and fetal death, even in those women who were previously immune. Severe malaria during pregnancy is more common during the first pregnancy (primigravida) and much less after multiple pregnancies (multigravid). Pregnant women are infected by parasites that sequester in the placenta and such sequestration contributes to growth retardation, infant mortality and severe anemia. Multigravid women develop antibodies that block the adhesion of infected erythrocytes to their placental receptor, chondroitin sulfate A (CSA). This interaction is mediated by specific var (PfEMP1) genes that bind to the host receptor CSA. The domain of the CSA-binding var gene that mediates adherence to CSA has been identified. This domain and potentially other parts of the molecule can give rise to development of anti malaria vaccines and therapeutics that will protect women from placental malaria, particularly during their first pregnancy.

Method for Generating NMR Relaxation Data and Identifying Ligands to Target Molecules From Multiple Field NMR Spectra

David Fushman, Nico Tjandra (NHLBI), David Cowburn
Serial No. 09/385,227 filed 27 Aug 1999

The present invention provides a nuclear magnetic resonance relaxation method of screening compounds for their ability to bind to target molecules and elicit site specific changes in the target molecule's structure. Specifically, this application pertains to a method of generating site specific nuclear relaxation data for target molecules and their ligands. These data can be used for exploration into the thermodynamic requirements of ligand binding, the calculation of structural constraints helpful in predicting the solution structure of a target molecule and its ligand complexes, and to design new ligands for target molecules.

Fast Displacement Encoding with Stimulated Magnetic Resonance Echoes by Sampling Both Components of a Stimulated Echo

Anthony H. Aletras, Han Wen (NHLBI)
Serial No. 60/147,314 filed 05 Aug 1999

The present invention provides a nuclear magnetic resonance method of phase contrast motion encoding. This methodology samples both the simulated-echo and the simulated-anti-echo by means of multiple 180 degree refocusing radiofrequency pulses. The pulses produced by the disclosed methods are compatible for reconstructing images without the need for elaborate data processing steps. By combining this method with pulses with unequal first order moments, dynamic range of motion measurements, in the heart, can be extended within the time period of a breath-hold in humans. Utilizing this powerful new methodology, a variety of diagnostic information can be learned about cardiac function in normal and diseased states.

MRI Contrast Agents Depending on Proton Chemical Exchange

Robert S. Balaban, Kathleen Ward, Anthony H. Aletras (NHLBI)

DHHS Reference No. E–240–98/0 filed 21 Apr 1999

Recently, methods have been developed to Magnetic Resonance Imaging (MRI) contrast using exogenous agents with exchangeable protons. These methods incorporate the use of selective reagents, such as sugars, amino acids, and nucleosides with appropriate proton exchange sites. Image contrast is generated by using saturation transfer techniques to selectively affect the water protons used in forming the MR image. The contrast agents developed do not contain metals or metal chelates. The agents have appropriate exchangeable proton sites which can be irradiated at known frequencies to obtain MRI images with specific contrast. This permits the image contrast to be turned off and on based on the irradiation scheme. This method also uses a controlled irradiation scheme to overcome the obstacle of broad proton resonance that limits contrast enhancement. In-Vivo data has shown the utility of this invention.

Oligomeric HIV–1 Envelope Glycoproteins

Patricia L. Earl, Chris C. Broder, Robert W. Doms, Bernard Moss (NIAID)

Serial Nos. 08/165,314 filed December 10, 1993; 08/805,889 filed March 3, 1997; 09/070,291 filed April 30, 1998; and 09/415,326 filed October 8, 1999

This invention embodies a method for generating antibodies to HIV–1 envelope glycoproteins, which could hold powerful implications toward both the diagnosis and the treatment of AIDS. Specifically, the method involves the expression of a soluble protein, gp140, and the generation of antibodies to this protein. gp140 is a recombinant version of gp160, a protein which normally is cleaved in vivo to generate two glycoprotein subunits which are expressed on the surface of the HIV–1 envelope. Unlike previously isolated versions of gp160, gp140 is purified in a manner which preserves the quaternary structural elements of the protein. Due to the conserved nature of these structural elements, antibodies generated against gp140 may be more broadly reactive against various forms of AIDS than other antibodies generated to date.

Dated: April 17, 2000.

Jack Spiegel,

Director, Division of Technology Development and Transfer, Office of Technology Transfer, National Institutes of Health.

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Hybrid Adeno-Retroviral Vector for the Transformation of Cells

C Zheng, B O'Connell, BJ Baum (NIDCR)
Serial No. E–258–98/0 filed 31 Jan 2000

The invention described and claimed in this patent application provides for novel hybrid vectors which may be used for cell transformation, either in vivo or in vitro. The hybrid vectors have an adenoviral backbone with retroviral long terminal repeats (LTRs). Such vectors are capable of transforming dividing or non-dividing cells and integrate stably into the chromosome providing a means of efficient, reliable, long-term gene expression. The vector was packaged as a recombinant adenovirus and delivered to the target cell. Unlike other chimeric or hybrid vector systems, only a single vector is required to deliver a transgene of interest, and retroviral structural proteins are not required.

This work has been published in part in Nature Biotechnology Zheng, et al. 18(2): 176–180 (Feb 2000).

Calcium Channel Compositions and Methods of Use Thereof

MI Lerman (NCI) *et al.*
Serial No. 09/470,443 filed 22 Dec 1999 and 60/114,359 filed 30 Dec 1998 (now abandoned)

This invention described in this patent application relates to the identification, isolation and cloning of a three cDNAs identified during a search of the short arm of chromosome 3 for a tumor suppressor gene (TSG) associated with lung cancer. The cDNA's are alternative isoforms which encode a protein which functions as a subunit of L-type voltage-dependent calcium channel. Type L voltage-dependent calcium channels represent one of five families of calcium channels, L, R, P, N, Q, which have been identified. Type L voltage-dependent calcium channels are found in a wide variety of tissues including the brain, muscle and the endocrine system.

The gene has been mapped to the short arm of chromosome 3 at 3p21.3. The gene, which corresponds to this cDNA is an alpha2delta-2 (α2δ-2) subunit, and has been shown to be deleted in lung and breast cancer. The scientists have demonstrated that the expression of this calcium channel has been shut off in lung cancer cells and hypothesize that this may lead to a malignant phenotype. Other cancers which may be associated with this α2δ-2 subunit include cervical cancer and head and neck carcinoma. Other non-malignant diseases which may also be associated with this α2δ-2 subunit include CNS diseases and cardiovascular diseases.

Possible applications of this technology include its use in drug screening assays; its use as an early diagnostic marker and/or as a prognostic or treatment indicator; its use in gene therapy where defective cells would be reconstituted with the gene and as a therapeutic agent for clearing autoantibodies which develop toward the alpha2delta-2 subunit in the disease Lambert-Eton myasthenia syndrome.

Monoclonal Antibody Against Met Protein

G Vande Woude, M Oskarsson, J Resau, S Rulong, Y Chui (NCI–FCRDC)
Serial No. 60/168,835 filed 03 Dec 1999

The invention described in this application relates to the Hepatocyte Growth Factor/Scatter Factor/Tumor Cytotoxic Factor (HGF/SF/F–TCF)-met/Hepatocyte Growth Factor Receptor